Tuesday, March 5, 1991
Poster Displayed: 9:00AM–12:00NOON
Author Present: 10:00AM–11:00AM
Hall F, West Concourse
Myocardial Ischemia: Experimental

THE ROLE OF SODIUM INFLUX DURING GLOBAL ISCHEMIA ON CONTRACTURE MYOCARDIAL INJURY

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To investigate the role of Na^+ and Ca^{2+} influx during global ischemia on contracture myocardial injury, we studied the effects of lidocaine(0.2mM) and verapamil(0.5μM) in 40 minute(min) ischemia of perfused rat hearts using ^{23}Na and ^{31}P magnetic resonance spectroscopy. Drugs were given for 5min prior to the start of ischemia. Each drug reduced cardiac work(%LV developed pressure(DP) x heart rate(HR) lidocaine;66±4%, verapamil;55±5%). During ischemia, each drug delayed the onset of a rise in resting tension(RT) and reduced the rise in RT, compared with no-treatment (control). Lidocaine reduced a rise in intracellular Na^+ level($[Na^+]i$) but verapamil did not. After reperfusion, lidocaine reduced a rise in RT and maintained higher levels of cardiac work and high energy phosphate than control, although the protective effects of verapamil were not obvious. Ca^{2+} overload is supposed to cause contracture myocardial injury. In this study, contracture myocardial injury is related with a rise in $[Na^+]i$ due to Na^+ influx during ischemia. It suggests that Ca^{2+} overload during ischemia and especially after reperfusion is mainly due to Ca^{2+} influx through Ca^{2+}-Na^+ exchange accelerated by a rise in $[Na^+]i$, not through slow Ca^{2+} channel.

		mean±SE(n=8)	control	lidocaine	verapamil
%$[Na^+]i$(%)	ischemia	40min	853±90	459±74*	637±93
RT(mmHg)	ischemia	40min	28± 7	16± 4	25± 7
RT(mmHg)	reperfusion	5min	62±10	18± 6**	43± 5
%LVDPxHR(%)	reperfusion	60min	56± 8	80±10	57± 7
%PC/(PC+Pi)	reperfusion	60min	28± 2	49± 4**	37± 3

PC:phosphocreatine Pi:inorganic phosphate *:p<.02 **:p<.01

HEAT SHOCK PROTEIN INDUCTION BY WHOLE BODY HYPERTHERMIA - A ROLE FOR IMPROVED MYOCARDIAL SALVAGE AFTER ISCHEMIA AND REPERFUSION?

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To test the hypothesis that the heat shock response is associated with improved myocardial salvage after ischemia and reperfusion, rats treated with prior hyperthermia (H) (n=60) and controls (C) (n=60) were subjected to either 35 or 45 min of left coronary artery (LCA) occlusion and 120 min of reflow. Ventricular samples from H rats (n=7) showed marked induction of 72 kDa heat shock protein (HSP72), determined by Western blot analysis, while C rats (n=7) showed no HSP72 induction. Compared to C rats (n=27), H rats (n=26) subjected to 35 min LCA occlusion and 2 hrs of reflow had reduced infarct size determined by TTC staining (8.4±1.7% vs 15.5±1.9%, p=0.007, mean±SEM, infarct mass/LV mass). There were no differences in HR, LV systolic pressure, LV dP/dt, or RPP between H (n=10) and C (n=11) rats during ischemia. After 45 min of LCA occlusion and reflow, there was a trend towards infarct size reduction in H (n=34) vs C (n=33) rats that was not significant (16.9±1.8% vs 19.2±1.6%, p=NS). In conclusion, rats treated with prior hyperthermia show improved myocardial salvage after 35 but not 45 minutes of LCA occlusion and reflow. This improved salvage is independent of the hemodynamic determinants of myocardial oxygen demand during ischemia and may be related to prior HSP72 induction in the heart.

CRITICAL VALUE OF REGIONAL MYOCARDIAL BLOOD FLOW NEEDED TO PRESERVE CELL MEMBRANE FUNCTION

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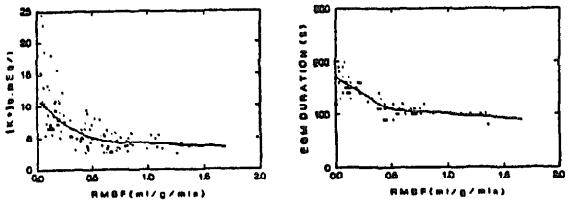
Myocardial ischemia due to acute reduction of regional myocardial blood flow (RMBF) causes potassium efflux, increase in extracellular potassium concentration ($[K^+]_o$), and slowing of electrical propagation. We correlated local midmyocardial electrogram (EGM), $[K^+]_o$ and RMBF of ischemic and nonischemic areas in 17 dogs undergoing 15 min LAD ligation. $[K^+]_o$ was measured using K-sensitive electrodes and RMBF was measured using 15u radioactive microspheres in 1g full thickness myocardial samples (n=112) around the electrode sites. The plots show curvilinear relationships between RMBF and $[K^+]_o$ (r = -0.68) and between RMBF and EGM duration as % of baseline (r = -0.84).



Reduction of RMBF below a critical level of 0.5 ml/g/min was associated with progressive increases in $[K^+]_o$ and EGM duration. Thus, at RMBF < 0.5 ml/g/min, there was significant potassium efflux associated with slowing of electrical conduction.

ANTI-ARRHYTHMIC EFFECTS OF DIETARY MENHADEN OIL (MO) IN MYOCARDIAL ISCHEMIA-REPERFUSION

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We have investigated the effects of dietary fish oil on cardiac arrhythmias following ischemia-reperfusion both in vivo and in vitro. Weanling rats were fed purified diets for 4 weeks in which the lipid was replaced with either corn oil (CO) or menhaden oil (MO). For in vivo studies rats were subjected to 15 min of left coronary artery ligation followed by 6h reperfusion. The incidence of ventricular tachycardia and ventricular fibrillation (VF) was significantly reduced in vivo during the ischemic and reperfusion periods in rats fed MO vs CO ($p<0.01$). In vitro studies were performed in isolated perfused hearts in which the coronary artery was ligated for either 40 or 60 min followed by 30 min of reperfusion. The ischemic area was equivalent for both experimental groups (58 vs 59% of the LV, MO vs CO, respectively). A similar reduction in the incidence of VF was observed in hearts of rats fed MO in both the 40 and 60 min in vitro ischemia models ($p<0.05$). Dietary MO resulted in significant elevations in both the ratio of n-3/n-6 fatty acids and the unsaturation index in myocardial phospholipids ($p<0.01$). These data suggest an anti-arrhythmic effect for dietary MO which is evident in both in vivo and in vitro models of myocardial ischemia-reperfusion.